REMARKS

Claims 1-19 are pending. Favorable reconsideration is respectfully requested.

The rejections of Claims 1-2, 4-9, 11-15, 17-19 under 35 U.S.C. §102(b) and/or 35 U.S.C. §103(a) over Tokuyama et al B or AC ((B) U.S. 5,525,501 and (AC) the corresponding European application EP 0 474 965) are traversed.

Applicants wish to bring the Examiner's attention to paragraph [0023] of the present specification in which Applicants note that the N-acetyl amino acid racemase (AAR) from *Amycolatopsis orientalis* subspecies lurida is prepared by recombinant technology according to DE 19935268, which is incorporated by reference. DE 19935268 corresponds to U.S. 6,372,459 (copy enclosed). Applicants note that the Office has already acknowledged novelty of AAR from *Amycolatopsis orientalis* subspecies lurida over *Amycolatopsis* sp. TS-1, as disclosed in the cited reference EP 0 474 965 (Tokuyama et al AC) and evidenced by the face of U.S. 6,372,459. Moreover, since U.S. 5,525,501 (Tokuyama et al B) corresponds to EP 0 474 965 (Tokuyama et al AC), it is submitted that AAR from *Amycolatopsis orientalis* subspecies lurida is novel over *Amycolatopsis* sp. TS-1 disclosed in this reference, as well.

Applicants request withdrawal of these grounds of rejection.

The rejections of Claims 1-19 under 35 U.S.C. § 102(b) and/or under 35 U.S.C. §103(a) over Takahashi et al are traversed.

<u>Takahashi et al</u> disclose the enzymatic action of an amino acid racemase (AAR) and an amino acid acylase (AAA) on N^2 -acylamino acids of Formula I:

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$$X \longrightarrow NH \longrightarrow C \longrightarrow COOH$$
 H

(I)

wherein X is a carboxylic acid derived acyl which may be substituted, and R is a C_{1-20} alkyl which may be substituted (see column 2, lines 51-61).

In direct contrast, the claimed invention relates to a process of racemizing amino acids by contacting an AAR with an N-carbamoyl amino acid compound. The N-cabamoyl amino acid compound is shown in scheme 2 of the present specification and has the following general formula:

The Office has taken the position that the term "carboxylic acid derived acyl" as disclosed by <u>Takahashi et al</u> encompasses an N-carbamoyl amino acid. The Examiner's attention is directed to the attached pages of Ullmann's definition of carboxylic acid (Ullmann's Encyclopedia of Industrial Chemistry, Volume A5, 1986, VCH, page 235). In Ullmann, carboxylic acid derived acyls have the following formula:

$$R-C$$

Applicants respectfully submit that even the skilled artisan would acknowledge that the above-mentioned definition of "carboxylic acid derived acyl" would <u>not</u> encompass an N-carbamovl amino acid.

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Further, <u>Takahashi et al</u> disclose that the carboxylic acid acyls include and alkanoyl, a benzoyl, and an arylalkanoyl (column 2, lines 62-64). With respect to the permissible substituents. <u>Takahashi et al</u> state that they may include a halogen, a C₁₋₃ alkyl, a C₁₋₃ alkoxy, and a nitro group (column 2, lines 64-65). However, there is no hint whatsoever within <u>Takahashi et al</u> of an N-carbamoyl amino acid.

In order for a reference to anticipate an invention, the reference "must teach every element of the claim" (MPEP §2131). Accordingly, <u>Takahashi et al</u> do not anticipate the present invention.

Moreover. Applicants submit that <u>Takahashi et al</u> cannot even support a *prima facie* case of obviousness.

The "carboxylic acid derived acyl" of <u>Takahashi et al</u> and the N-carbamoyl amino acid of the present claims can not even be considered homologs of each other. The Federal Circuit has defined the parameters that may be considered in determining the proper use of chemical structure as the basis for obviousness rejections under 35 U.S.C. § 103 in *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992) (**copy enclosed**). The court cited the following examples of relationships that have given rise to a *prima facie* case of obviousness:

triorthoesters and tetraorthoesters:

stereoisomers:

adjacent homologs and structural isomers; and

acid and ethyl ester (Id., at 1943).

In the present case, there exists no motivation to modify the compounds disclosed by <u>Takahashi et al</u> to contain an N-carbamoyl amino acid, because the relationship between the claimed compounds and those disclosed by <u>Takahashi et al</u> fail to satisfy any of the abovementioned relationships to be defined as homologs by the Federal Circuit.

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In light of the above. Applicants submit that <u>Takahashi et al</u> fail to disclose or suggest racemizing an N-carbamoyl amino acid by an N-carbamoyl amino acid with AAR from *Amycolatopsis orientalis* subspecies lurida as presently claimed. Therefore, the present invention is neither anticipated by nor obvious in view of <u>Takahashi et al</u>.

Accordingly, withdrawal of these grounds of rejections is respectfully requested.

The rejections of Claims 1-19 under 35 U.S.C. §102(a) over <u>Verseck et al</u> and of Claims 1-19 under 35 U.S.C. §102(a) and/or under 35 U.S.C. §103(a) over <u>Drauz</u> are respectfully traversed on the ground that <u>Verseck et al</u> and <u>Drauz</u> may not be cited as prior art against the present application.

Specifically, <u>Verseck et al</u> was published on March 13, 2001 and <u>Drauz</u> was published on February 20, 2001. In contrast, the present application claims priority to DE 100 50 124.9, filed on October 11, 2000, over four months prior to publication of either <u>Verseck et al</u> or <u>Drauz</u>. To perfect their claim of priority. Applicants are filing herewith a certified English translation of DE 100 50 124.9. Applicants request that the Examiner acknowledge perfection of the claim to priority and entitlement to an earlier filing date of October 11, 2000. Based on the earlier filing date, <u>Verseck et al</u> and <u>Drauz</u> are not prior art against the present claims and the rejections over these references should be withdrawn.

The rejection of Claims 1-2, 4-9, 11-15, and 17-19 under 35 U.S.C. § 112. first paragraph, is traversed.

The Examiner has taken the position that the specification "does not teach "any and all such enzymes from *Amycolatopsis orientalis* subspecies lurida" (paper number 8, page 2). However, contrary to this assertion by the Examiner, the present claims require that the N-

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acetyl amino acid racemase (AAR) from *Amycolatopsis orientalis* subspecies lurida be used for the racemization reaction.

MPEP §2164.04 states:

"A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support."

In paragraphs [0023] to [0029], Applicants provide an explanation of the inventive method. Of particular note, in paragraph [0023], Applicants point to DE19935268 and note that this reference, which is incorporated by reference, provides variants of AAR from *Amycolatopsis orientalis* subspecies lurida prepared by recombinant technology. Also in this paragraph, the AAR is described to have little heavy metal ion dependence and low amino acid inhibition. Not only do the Applicants provide adequate disclosure to fully enable the skilled artisan to make the claimed compounds, in paragraphs [0031] to [0038], Applicants provide a detailed example demonstrating the inventive method may be performed. Therefore, the Applicants have met their burden of clearly defining the scope of the claimed method, including the AAR.

At no point does the Examiner offer any "reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support" as required by MPEP §2164.04. Therefore, the Examiner has not met the burden necessary to establish a lack of enablement, much less refute the showing above.

Accordingly, this ground of rejection is unsustainable and should be withdrawn.

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The rejection of Claims 1, 5, 6, 8, 12-14, and 18-19 under 35 U.S.C. §112, second paragraph, is obviated by appropriate amendment.

Consistent with the Examiner's helpful suggestion. Applicants have amended the claims to clarify the language. In view of these amendments, it is believed that this ground of rejection is no longer tenable.

Applicants request withdrawal of this ground of rejection.

Applicants note that the amendments made in response to the outstanding Office Action only serve to make minor grammatical changes and do not alter the claim scope in any way. Therefore, Applicants note that all of the presently pending claims have been fully searched on the merits. Therefore, any new ground of rejection cannot be reasonably considered to have been necessitated by Applicants' amendment. Accordingly, it is expected that any new ground of rejection would be in a new non-final Office Action.

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Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted.

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In re Jones (CA FC) 21 USPQ2d 1941

In re Jones

U.S. Court of Appeals Federal Circuit 21 USPQ2d 1941

Decided February 28, 1992 No. 91-1380

Headnotes

PATENTS

1. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Claimed novel salt of acid commonly known as "dicamba" is not so closely related in structure to substituted ammonium salts disclosed in prior patent as to be prima facie obvious, since claimed salt is primary amine with ether linkage, whereas diethanolamino salt disclosed in reference patent is secondary amine without ether linkage, since claimed salt is plainly acyclic or linear, whereas morpholino salt, which is only substituted ammonium salt of dicamba with ether linkage disclosed in reference patent, is cyclic in structure, and since isopropylamino salt disclosed in reference patent is primary amine, but has iso-structure quite different from that of claimed salt.

2. Patentability/Validity -- Obviousness -- Relevant prior art -- Particular inventions (§ 115.0903.03)

Claimed novel salt of acid commonly known as "dicamba" cannot be held prima facie obvious in

view of salts disclosed in prior patent, even though claimed salt is member of genus of substituted ammonium salts broadly disclosed in reference patent, since reference discloses potentially infinite genus of "substituted ammonium salts" of dicamba, and lists several such salts, but does not specifically disclose salt claimed in application, and since claimed salt is not sufficiently similar to those disclosed in reference as to render it prima facie obvious.

3. Patentability/Validity -- Obviousness -- Combining references (§ 115.0905)

Contention that one skilled in herbicidal art would have been motivated to use, with acid commonly known as "dicamba," substituted ammonium salt such as that disclosed in two prior references does not warrant holding that claimed substituted ammonium salt of dicamba for use as herbicide is prima facie obvious, since there is no suggestion for combining disclosures of those references either in references themselves, which are directed to shampoo additives and production of morpholine, respectively, or in knowledge generally available to those skilled in art.

Case History and Disposition:

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Appeal from the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences.

Patent application of Rita S. Jones, Michael T. Chirchirillo and Johnny L. Burns, serial no. 07/099,279 (the 2-(2 '-aminoethoxy)-ethanol salt of dicamba). From decision upholding rejection of only claim in application, applicants appeal. Reversed.

Attorneys:

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Harris A. Pitlock, associate solicitor (Fred E. McKelvey, solicitor, with him on brief: Richard E. Schafer, of counsel), for appellee.

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Judge:

Before Rich, Archer, and Clevenger, circuit judges.

Opinion Text

Opinion By:

Rich, J.

Rita S. Jones et al. (collectively Jones) appeal from the April 15, 1991 decision of the Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (Board), Appeal No. 90-1920, sustaining the rejection of claim 1, the only claim of application Ser. No. 07/099,279, titled "The 2-(2 '-Aminoethoxy) -- Ethanol Salt of Dicamba," as unpatentable under 35 USC 103. We conclude that the PTO has not presented a *prima facie* case of obviousness, and therefore *reverse*.

The Invention

The Claimed invention is a novel salt of 2-methoxy-3, 6-dichlorobenzoic acid, which acid is commonly referred to as "dicamba." A known herbicide, dicamba has typically been sold in the form of its known dimethylamine salt.

The sole claim of the application on appeal reads:

1. The 2-(2 '-aminoethoxy) ethanol salt of dicamba.

The claimed salt has the following structure:

The Rejection

Claim 1 stands rejected as obvious in view of the combined teachings of the following references:

Richter, U.S. Patent No. 3,013,054, Dec. 12, 1961

Moyle et al., U.S. Patent No. 3,056,669, Oct. 2, 1962

Balassa, U.S. Patent No. 3,725,031, Apr. 3, 1973

Zoravan et al., 88 Chem. Abstracts No. 52300j, 1978

Wideman, 86 Chem. Abstracts No. 43711a, 1977

Richter, which all agree is the closest prior art, discloses dicamba in free acid, ester, and salt forms, for use as a herbicide. Among the salt forms disclosed are substituted ammonium salts, a

genus which admittedly encompasses the claimed salt. Richter does not specifically disclose the claimed 2-(2 '- aminoethoxy) ethanol salt, however. Most notably, Richter discloses (emphasis and bracketed word ours):

Compositions in which X is substituted ammonium are amine salts of 2-methoxy-3. 6-dichlorobenzoic acid [dicamba] and are prepared by the addition of the free acid to various amines. Typical amines which can be used to prepare such amine salts are dimethylamine, trimethylamine, triethylamine, diethanolamine, triethanolamine, isopropylamine, morpholine, and the like. The resulting products are, respectively, the dimethylamino, trimethylamino, triethylamino, diethanolamino, triethanolamino, isopropylamino, and morpholino salts of 2-methoxy-3, 6-dichlorobenzoic acid.

Zorayan teaches the amine (H [inf 2] N (CH [inf 2] CH [inf 2] O) [inf 2] H) used to make the claimed salt, as well as the use of that amine in the preparation of surfactants for shampoos, bath preparations, and emulsifiers.

Wideman also teaches the amine disclosed in Zorayan.

The content of the remaining references is unnecessary to our decision.

The Board upheld the examiner's rejection of claim 1 as obvious, finding that the claimed 2-2 '-aminoethoxy') ethanol salt of dicamba and the diethanolamine salt of dicamba specifically disclosed by Richter were "closely related in structure," and that based upon the expectation that "compounds similar in structure will have similar properties," a *prima facie* case of obviousness had arisen. The Board found that Jones' rebuttal evidence (Rule 132 declarations and data reported in the specification) failed to "compare the claimed subject matter with the closest prior art," and accordingly did not serve to rebut the *prima facie* case. This appeal followed.

Analysis

The Solicitor contends that the claimed salt falls within the genus of substituted amine salts of dicamba disclosed by Richter, and that, like Richter's genus, the claimed compound has herbicidal activity. Thus, the Solicitor urges, under the circumstances of this case, (1) the genus/species relationship and (2) the common utility of the claimed and prior art compounds support the Board's holding of *prima facie* obviousness. Moreover, the Solicitor adds, although the claimed compound is neither a homolog nor a position isomer of those salts specifically disclosed in Richter, it is structurally similar thereto, particularly the diethanolamino salt noted by the Board.

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The question of "structural similarity" in chemical patent cases has generated a body of patent law unto itself. 1 Particular types or categories of structural similarity without more have, in past cases, given rise to *prima facie* obviousness; *see*, *e.g.*, *In re Dillon*, 919 F.2d 688, 692-94, 16 USPQ2d 1897, 1900-02 (Fed. Cir. 1990) (tri-orthoesters and tetra-orthoesters). *cert. denied*,

U.S. ____, 111 S. Ct. 1682 (1991); In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers): In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) (adjacent homologs and structural isomers): In re Hoch, 428 F.2d 1341, 166 USPQ 406 (CCPA 1970) (acid and ethyl ester). However, none of these types of structural similarity are involved here. And in any event, this court has previously stated that generalization is to be avoided insofar as specific structures are alleged to be prima facie obvious one from the other. In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

[1] On the basis of the record before us, we cannot sustain the Board's conclusion that the claimed salt and the diethanolamino salt disclosed by Richter are so "closely related in structure" as to render the former *prima facie* obvious in view of the latter. The claimed salt is a primary amine with an ether linkage. The diethanolamino salt disclosed by Richter is a secondary amine, without an ether linkage:

In addition, the only substituted ammonium salt of dicamba expressly disclosed by Richter having an ether linkage is the morpholino salt, which is *cyclic* in structure:

The claimed salt is, plainly, a cyclic; i.e., linear. Lastly, while the isopropylamino salt disclosed by Richter is a primary amine, as is the claimed salt, its iso-structure is quite different:

[2] The lack of close similarity of structure is not negated by the fact that the claimed salt is a member of Richter's broadly disclosed genus of substituted ammonium salts of dicamba. The Solicitor contends that " [t]he relative size of the genus disclosed by the prior art would not appear to be a controlling factor in determining whether a *prima facie* case of obviousness exists for a species encompassed within the described genus," citing Merck & Co. v. Biocraft Labs., Inc., 874 F.2d 804, 806-09, 10 USPQ2d 1843, 1845-48 (Fed. Cir.), cert. denied. U.S. , 110 S. Ct. 498 (1989). We decline to extract from Merck the rule that the Solicitor appears to suggest -- that regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it. In *Merck*, at issue on appeal was whether claims to a composition of two diuretics, amiloride and hydrochlorothiazide, present in a particular "medically synergistic" weight ratio, would have been obvious in view of a specific prior art disclosure of amiloride in combination with hydrochlorothiazide, one of 1200 such combinations disclosed in the prior art reference. Id. at 806. 10 USPQ2d at 1845. Based on the facts before it, including evidence at trial that the experimentation needed to arrive at the claimed dosage was "nothing more than routine," *ld.* at 809, 10 USPQ2d at 1847, the court affirmed the trial court's determination of obviousness. In contrast, though Richter discloses the potentially infinite genus of "substituted ammonium salts" of dicamba, and lists several such

salts, the salt claimed here is not specifically disclosed. Nor, as we have explained above, is the claimed salt sufficiently similar in structure to those specifically disclosed in Richter as to render it *prima facie* obvious. Every case, particularly those raising the issue of obviousness under section 103, must necessarily be decided upon its own facts.

[3] The Solicitor points out that, given the breadth of forms of dicamba (free acid, ester, or salt) disclosed by Richter as having herbicidal utility, one of ordinary skill in the art would appreciate that the dicamba group has significance with respect to imparting herbicidal activity to dicamba compounds. Thus, the Solicitor contends, one skilled in the art would have been motivated to use, with dicamba, substituted ammonium salts made from a known amine, such as the amine disclosed by Zorayan and Wideman, and would have expected such a salt to have herbicidal activity. Before the PTO may combine the disclosures of two or more prior art references in order to establish *prima facie* obviousness, there must be some sug

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gestion for doing so, found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). We see no such suggestion in Zorayan, which is directed to shampoo additives, nor in Wideman, which teaches that the amine used to make the claimed compound is a byproduct of the production of morpholine. Nor does the broad disclosure of Richter fill the gap, for the reasons discussed above.

Conspicuously missing from this record is any *evidence*, other than the PTO's speculation (if it be called evidence) that one of ordinary skill in the herbicidal art would have been motivated to make the modifications of the prior art salts necessary to arrive at the claimed 2-(2 '-aminoethoxy) ethanol salt. *See Grabiak*, 769 F.2d at 731-32, 226 USPQ at 872 ("[I]n the case before us there must be adequate support in the prior art for the [prior art] ester/ [claimed] thioester change in structure, in order to complete the PTO's *prima facie* case and shift the burden of going forward to the applicant."): *In re Lalu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984) ("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.")

Conclusion

We conclude that the PTO did not establish a *prima facie* case of obviousness, and thus did not shift to Jones the burden of coming forward with unexpected results or other objective evidence of non-obviousness. Accordingly, the decision of the Board is *REVERSED*.

Footnotes

Footnote 1. See generally Helmuth A. Wegner, "Prima Facie Obviousness of Chemical Compounds," 6 Am. Pat. L. Assoc. O. J. 271 (1978).

- End of Case -

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Carboxylic Acids, Aliphatic

Many industrially important aliphatic carboxylic acids and derivatives are treated in separate articles Acetic Acid. Acrylic Acid. Adipic Acid. Chloroacetic Acids. Citric Acid. Crotonic Acid. Dicarboxylic Acids. Aliphatic. Ethylenediaminetetraacetic Acid. Fatty Acids. Formic Acid. Glyoxal and Glyoxylic Acid. Hydroxycarboxylic Acids and Oxocarboxylic Acids. Lactic Acid. Maleic and Fumaric Acid. Malonic Acid. Mercaptoacetic Acid. Methacrylic Acid. Nitrilotriacetic Acid. Naphthenic Acids. Oxalic Acid. Propionic Acid. Sorbic Acid. Tartaric Acid.

WILHELM RIEMENSCHNEIDER, retired from Hoechst Aktiengesellschaft, Frankfurt, Federal Republic of Germany

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Aliphatic carboxylic acids have the general formula [0]

R C CH

where R is H or a straight-chain or branchedchain alkyl group. The first three members of this homologous series, formic, acetic, and propionic acid, are exceptionally important and are discussed in separate articles. Similarly, acids containing 12 or more carbon atoms are described separately under \rightarrow Fatty Acids. The unsaturated acids acrylic, methacrylic, crotonic, and sorbic acid are also treated separately, as are chloroacetic and oxo- and hydroxycarboxylic acids. The continuing scientific importance of the C_4 - C_{11} carboxylic acids arises from their functions in the metabolism of plants and animals (see Chap. 3). The great commercial value of these acids, and particularly of their salts and esters, is based on their synthetic utility (see Chap. 8).

Numerous aliphatic carboxylic acids were first obtained from natural sources in the 19th century along with many other natural products. However, these natural sources, which usually yielded straight-chain acids containing an even number of carbon atoms, have since been replaced by large-scale synthetic operations (see Chaps 4 and 9)

